Claims

1. A particle derivative of at least one form of high density lipoprotein comprising apolipoprotein A-1 and phospholipids wherein the particle derivative is formed by exposing a mixture of the high density lipoprotein and low density lipoprotein to a lipid removing agent, wherein the exposure does not substantially modify the low density lipoprotein.

2. The particle derivative of claim 1, wherein the particle derivative has a lower content of cholesterol than the high density lipoprotein.

3. The particle derivative of claim 1,wherein the particle derivative has physical, chemical, or biological properties substantially similar to naturally formed pre-beta$_1$ high density lipoprotein, naturally formed pre-beta$_2$ high density lipoprotein or naturally formed pre-beta$_3$ high density lipoprotein.

4. The particle derivative of claim 1, wherein the lipid removing agent is an ether or a combination of an alcohol and an ether.

5. The particle derivative of claim 4, wherein the ether is di-isopropyl ether

6. The particle derivative of claim 4, wherein the alcohol is n-butanol.

7. The particle derivative of claim 1, wherein the lipid removing agent is a mixture of sevoflurane and n-butanol.

8. The particle derivative of claim 1, wherein the exposure is achieved by an exposure process comprising the steps of:

a. mixing the lipid removing agent with a mixture of the high density lipoprotein and the low density lipoprotein to create a mixture of the particle derivative, lipids, the lipid removing agent, and the low density lipoprotein;

b. separating the lipid removing agent and lipids from the mixture of the particle derivative, the lipids, the lipid removing agent, and the low density lipoprotein; and,

c. collecting the particle derivative and low density lipoprotein.

9. The particle derivative of claim 8, wherein the lipid removing agent comprises a mixture of 95 parts sevoflurane and 5 parts n-butanol.

10. The particle derivative of claim 8, wherein the mixing is performed using a static mixer.

11. The particle derivative of claim 8, wherein the separation is performed using a charcoal column.

12. The particle derivative of claim 8, further comprising the steps of:

a. connecting a patient to a device for withdrawing blood;
b. withdrawing blood containing blood cells from the patient;
c. separating blood cells from the blood to yield a fraction wherein the fraction contains a mixture of the high density lipoprotein and the low density lipoprotein; and,
d. mixing the lipid removing agent with the fraction.

13. A particle derivative of at least one form of high density lipoprotein comprising apolipoprotein A-1 and phospholipids wherein the particle derivative is formed by first removing low density lipoprotein from a mixture of the high density lipoprotein and the low density lipoprotein and subsequently exposing the mixture to a lipid removing agent.

14. The particle derivative of claim 13, wherein the particle derivative has a lower content of cholesterol than the high density lipoprotein.

15. The particle derivative of claim 13, wherein the lipid removing agent is an ether or a combination of an alcohol and an ether.

16. The particle derivative of claim 15, wherein the ether is di-isopropyl ether

17. The particle derivative of claim 15, wherein the alcohol is n-butanol.

18. The particle derivative of claim 13, wherein the lipid removing agent is a mixture of sevoflurane and n-butanol.

19. The particle derivative of claim 13, wherein the exposure is achieved by an exposure process comprising the steps of:

a. separating the low density lipoprotein from a mixture of the high density lipoprotein and the low density lipoprotein;
b. mixing the lipid removing agent with the high density lipoprotein to create a mixture of the particle derivative, lipids, and the lipid removing agent;
c. separating the lipid removing agent and lipids from the mixture of the particle derivative, the lipids, and the lipid removing agent; and,
d. collecting the particle derivative.

20. The particle derivative of claim 19, wherein the lipid removing agent comprises a mixture of 95 parts sevoflurane and 5 parts n-butanol.

21. The particle derivative of claim 19, wherein the separation of the low density lipoprotein is performed using an apheresis device.

22. The particle derivative of claim 19, wherein the mixing is performed using a static mixer.

23. The particle derivative of claim 19, wherein the separation of the lipid removing agent and the lipids is performed using a charcoal column.

24. The particle derivative of claim 19, further comprising the steps of:

a. connecting a patient to a device for withdrawing blood;
b. withdrawing blood containing blood cells from the patient ; and,
c. separating blood cells from the blood to yield a fraction wherein the fraction contains a mixture of the high density lipoprotein and the low density lipoprotein.

25. A particle derivative of a pre-beta form of high density lipoprotein comprising a protein shell and a lipid bilayer substantially devoid of cholesterol wherein the particle derivative is discoidal in shape and is formed by first removing low density lipoprotein from a mixture of the high density lipoprotein and the low density lipoprotein and subsequently exposing the mixture to a lipid removing agent.

26. The particle derivative of claim 25, wherein the exposure is achieved by an exposure process comprising the steps of:

a. mixing the lipid removing agent with a mixture of the high density lipoprotein and the low density lipoprotein to create a mixture of the particle derivative, lipids, the lipid removing agent, and the low density lipoprotein;

b. separating the lipid removing agent and the lipids from the mixture of the particle derivative, the lipids, the lipid removing agent, and the low density lipoprotein; and,

c. collecting the particle derivative and the low density lipoprotein.

27. The particle derivative of claim 26, wherein the lipid removing agent comprises a mixture of 95 parts sevoflurane and 5 parts n-butanol.

28. The particle derivative of claim 26, further comprising the steps of:

a. connecting a patient to a device for withdrawing blood;

b. withdrawing blood containing blood cells from the patient ;

c. separating the blood cells from the blood to yield a fraction wherein the fraction contains a mixture of the high density lipoprotein and the low density lipoprotein; and,

d. mixing the lipid removing agent with the fraction.

29. A particle derivative of a pre-beta form of high density lipoprotein comprising a protein shell and a lipid bilayer substantially devoid of cholesterol wherein said particle derivative is discoidal in shape and formed by exposing a mixture of the high density lipoprotein and low density lipoprotein to a lipid removing agent wherein the exposure does not substantially modify the low density lipoprotein.

30. A method for making a particle derivative of at least one form of high density lipoprotein wherein the particle derivative comprises a protein shell and a lipid bilayer comprising the steps of:

a. connecting a patient to a device for withdrawing blood;

b. withdrawing blood containing blood cells from the patient ;

c. separating the blood cells from the blood to yield a blood fraction containing high density lipoprotein and low density lipoprotein;

d. separating the low density lipoprotein from the blood fraction;
e. mixing the blood fraction with a lipid removing agent which removes lipids associated with the lipid bilayer of the high density lipoprotein to yield a mixture of lipid, the lipid removing agent, and the particle derivative;
f. separating the particle derivative from the lipid and the lipid removing agent; and,
g. delivering the particle derivative to the patient.

31. The method of claim 30, wherein steps c through f occur remote from the subject.

32. The method of claim 30, wherein the separation of the low density lipoprotein from the blood fraction is performed using an apheresis device.

33. The method of claim 30, wherein the lipid removing agent is at least one of an ether, di-isopropyl ether, sevoflurane, a combination of an alcohol and an ether, or a combination of a sevoflurane and an alcohol.

34. The method of claim 33, wherein the lipid removing agent is a mixture of sevoflurane and n-butanol.

35. The method of claim 34, wherein the mixture comprises 95 parts sevoflurane and 5 parts n-butanol.

36. The method of claim 30, wherein the step of separating the particle derivative from the lipid and the lipid removing agent is achieved by at least one of an absorbent, separator, centrifuge, or charcoal column.

37. The method of claim 36, wherein the at least one of an absorbent, separator, centrifuge, or charcoal column does not modify the protein shell of the particle derivative.

38. The method of claim 30, wherein the particle derivative is first recombined with the blood cells before delivering the particle derivative to the patient.

39. The method of claim 30, wherein the mixing is performed using at least one of a static mixer, vortexer or centrifuge.

40. A method for making a particle derivative of at least one form of high density lipoprotein wherein the particle derivative comprises a protein shell and a lipid bilayer comprising the steps of:

a. connecting a patient to a device for withdrawing blood;
b. withdrawing blood containing blood cells from the patient ;
c. separating the blood cells from the blood to yield a blood fraction containing high density lipoprotein and low density lipoprotein;
d. mixing the blood fraction with a lipid removing agent which removes lipids associated with a lipid bilayer of the high density lipoprotein without substantially modifying the low density lipoprotein to yield a mixture of lipid, the lipid removing agent, the particle derivative, and the low density lipoprotein;
e. separating the particle derivative and the low density lipoprotein from the lipid and the lipid removing agent; and,
f. delivering the particle derivative and the low density lipoprotein to the patient.

41. The method of claim 40, wherein steps c through e occur remote from the subject.

42. The method of claim 40, wherein the lipid removing agent is at least one of an ether, di-isopropyl ether, sevoflurane, a combination of an ether and an alcohol, or a combination of sevoflurane and an alcohol.

43. The method of claim 42, wherein the lipid removing agent is a mixture of sevoflurane and n-butanol.

44. The method of claim 43, wherein the mixture comprises 95 parts sevoflurane and 5 parts n-butanol.

45. The method of claim 40, wherein the step of separating the particle derivative and low density lipoprotein from the lipid and lipid removing agent is achieved by at least one of an absorbent, separator, centrifuge, or charcoal column.

46. The method of claim 45, wherein the at least one of an absorbent, separator, centrifuge, or charcoal column does not modify the protein shell of the particle derivative.

47. The method of claim 40, wherein the particle derivative and the low density lipoprotein are first recombined with the blood cells before delivering the particle derivative and the low density lipoprotein to the patient.

48. The method of claim 40, wherein the mixing is performed using at least one of a static mixer, vortexer or centrifuge.

49. A method for modifying at least one form of high density lipoprotein contained in plasma, serum, or other suitable blood fraction of a patient, comprising the steps of:

a. obtaining a blood fraction containing high density lipoprotein and low density lipoprotein from the patient;
b. separating the low density lipoprotein from the blood fraction;
c. mixing the blood fraction with a lipid removing agent which removes lipids from the high density lipoprotein to yield a mixture of lipid, lipid removing agent, and modified high density lipoprotein;
d. separating the modified high density lipoprotein from the lipid and the lipid removing agent; and,
e. delivering the modified high density lipoprotein to the patient.

50. A method for modifying at least one form of high density lipoprotein contained in plasma, serum, or other suitable blood fraction of a patient, comprising the steps of:

a. obtaining a blood fraction containing high density lipoprotein and low density lipoprotein from the patient;
b. mixing the blood fraction with a lipid removing agent which removes lipids associated with the high density lipoprotein without substantially modifying the low density lipoprotein to yield a mixture of lipid, the lipid removing agent, modified high density lipoprotein, and the low density lipoprotein;
c. separating the modified high density lipoprotein and the low density lipoprotein from the lipid and the lipid removing agent; and,

d. delivering the modified high density lipoprotein and the low density lipoprotein to the patient.

51. A method of modifying a protein distribution in a fluid wherein the protein distribution has a first state, the first state having alpha high density lipoproteins and pre-beta high density lipoproteins, comprising the steps of:

exposing the fluid to a lipid removing agent wherein the exposure modifies the protein distribution from the first state into a second state, the second state having an increased concentration of pre-beta high density lipoprotein relative to the first state; and,

removing the lipid removing agent from the biological fluid.

52. The biological fluid of claim 51 wherein the biological fluid is plasma.

53. A method of enhancing an ABCA1 pathway of a patient with a first protein distribution, the first protein distribution having a concentration of pre-beta high density lipoproteins relative to total protein, comprising the step of modifying a fluid containing the first protein distribution by exposing the fluid to a lipid removing agent, wherein the modification increases the concentration of pre-beta high density lipoprotein relative to the total protein, and introducing the fluid into the patient.

54. The biological fluid of claim 53 wherein the biological fluid is plasma.

55. A method of modifying a protein distribution in a fluid wherein the protein distribution has a first state, the first state having more alpha high density lipoprotein than pre-beta high density lipoprotein, comprising the steps of:

exposing the fluid to a lipid removing agent wherein the exposure modifies the protein distribution from the first state into a second state, the second state having more pre-beta high density lipoprotein than alpha high density lipoprotein; and,

removing the lipid removing agent from the biological fluid.

56. The method of claim 55, wherein ApoB proteins associated with low density lipoproteins are in the fluid

57. The method of claim 56, wherein the ApoB proteins are substantially unaffected by the lipid removing agent.

58. The biological fluid of claim 55, wherein the biological fluid is plasma.

59. A method of changing blood rheology of a patient with impaired blood circulation whereby the plasma, serum, or other suitable blood fraction of the patient has been treated by a method as claimed in claim 49.

60. A method of changing blood rheology of a patient with impaired blood circulation whereby the plasma, serum, or other suitable blood fraction of the patient has been treated by a method as claimed in claim 50.

61. A method for regression of atherosclerosis in a patient whereby the plasma, serum, or other suitable blood fraction from the patient is treated by a method as claimed in claim 49.

62. A method for regression of atherosclerosis in a patient whereby the plasma, serum, or other suitable blood fraction from the patient is treated by a method as claimed in claim 50.

63. A kit for performing any of the methods of claims 30 to 58 comprising:

a. a high density lipoprotein source container;
b. a lipid removing agent source container;
c. a mixer comprising at least one of a static mixer, vortexer, or centrifuge;
d. a separator comprising at least one of an absorbent, separator, centrifuge, or charcoal column;
e. an output container for storing a particle derivative of the high density lipoprotein; and,
f. a plurality of tubing and a plurality of valves for controlling the flow of high density lipoprotein from the high density lipoprotein source container and lipid removing agent from the lipid removing agent source container to the mixer, for controlling the flow of the mixture of lipid removing agent, lipid, and derivative to the

separator, and for controlling the flow of the particle derivative to the output container.

64. A kit for performing any of the methods of claims 30 to 58 comprising:

a. a high density lipoprotein source container;
b. a lipid removing agent source container;
c. a mixer comprising at least one of a static mixer, vortexer, or centrifuge;
d. a separator comprising at least one of an absorbent, separator, centrifuge, or charcoal column;
e. an output container for storing modified high density lipoprotein; and,
f. a plurality of tubing and a plurality of valves for controlling the flow of high density lipoprotein from the high density lipoprotein source container and lipid removing agent from the lipid removing agent source container to the mixer, for controlling the flow of the mixture of lipid removing agent, lipid, and modified high density lipoprotein to the separator, and for controlling the flow of modified high density lipoprotein to the output container.

65. A method of enhancing cellular cholesterol efflux comprising administration of a modified HDL particle to a patient.

66. The method of Claim 65, further comprising administration of a statin, an inhibitor of cholesterol uptake, a fibric acid derivative, nicotinic acid, a bile acid-binding resin or a combination thereof.

67. A particle comprising a modified HDL particle, wherein the modified HDL particle has a relatively normal complement of Apo A-1 and phospholipid and substantially reduced cholesterol compared to an HDL particle before modification.

68. A particle comprising a modified HDL particle, wherein the modified HDL particle has a relatively normal complement of Apo A-1 and substantially reduced cholesterol and phospholipid compared to an HDL particle before modification.

69. A biological fluid capable of enhancing an ABCA1 pathway of a patient wherein said biological fluid is made by modifying a fluid having a first concentration of pre-beta high density lipoprotein relative to total protein wherein the modification increases the concentration of pre-beta high density lipoprotein relative to total protein.

70. The biological fluid of claim 69 wherein the biological fluid is plasma.

71. A biological fluid comprising a modified protein distribution wherein the biological fluid had a first state, the first state having alpha high density lipoproteins and pre-beta high density lipoproteins, and wherein the biological fluid has a second state after being exposed to a lipid removing agent, the second state having an increased concentration of pre-beta high density lipoprotein relative to the first state.

72. The biological fluid of claim 71 wherein the biological fluid is plasma.